Essentially, Applicants respectfully maintain that sufficient evidence has been submitted which substantiates the novel, non-obvious features of the invention, and also with respect to the efficacy of the claimed method.

As previously argued, the present inventors have surprisingly discovered that particular cationic liposomol formulations containing antisense oligos which are specific to oncogenes expressed by tumor tissue, when administered to patients undergoing radiotherapy, renders tumor cells more susceptible to radiotherapy. While not wanting to be bound by their belief, it is hypothesized that the oligo containing cationic liposomal formulations renders tumor cells more susceptible to apoptosis, perhaps by triggering the expression of "death" genes.

Applicants note that with respect to such discovery, the Examiner has acknowledged the inventiveness of this invention in the context of one antisense oligonucleotide, which is specific to raf-1. The only aspect wherein the subject claims are broader than that allowed in the parent application resides in the fact that the claims generically encompass the use of antisense oligos targeted against an oncogene expressed by a particular tumor.

With respect thereto, as the Examiner can well appreciate, the use of antisense therapy to treat cancerous tumors is hardly novel. As evidence of this fact, Applicants note that a search of the U.S. Patent database revealed that 59 patents have issued from 1996 to the present date containing claims directed to antisense therapy of cancer.

Of these patents, one is believed to be directly on point to the facts at hand. Specifically, U.S. Patent 6,165,440 issued December 26, 2000 is directed toward a method for enhancing the delivery of an anti-cancer drug to a solid tumor by injecting nanoparticles or microparticles into the tumor by IV administration and irradiation, with administration of an anti-cancer drug. Moreover, of the list of suitable anti-cancer drugs in the claims, anti-sense oligos are specifically included.

Presumably there, the Examiner properly concluded that the Patentee therein was entitled broad scope with respect to the anti-cancer drug as this did not constitute the significant novel and non-obvious aspect of the invention. Rather, the generic discovery of their patented invention involved a novel therapeutic combination that potentiated efficacy.

The present specification involves a very similar set of facts. Essentially, the present inventors have discovered that a particular cationic liposomal delivery system potentiates the efficacy of an antisense oligos, particularly by allowing for the specific internalization of

tumor cells that express a gene bound by said oligo. Thereby such cells are rendered more susceptible to radiotherapy.

This enhancement has been demonstrated both in vitro and in vivo, in an accepted tumor model, and in ongoing human clinical studies. In view of this surprising and beneficial discovery, Applicants respectfully submit that it would be unreasonable and unfair to limit the scope of the allowed claims to a particular antisense oligo, especially as numerous patents have issued to date, substantiating the growing acceptance by the Patent Office, and those skilled in the art, that antisense oligo therapy is effective.

Therefore, based on the foregoing, the Examiner is respectfully requested to reconsider the propriety of the rejection, especially since it does not take into sufficient account the full scope of the discovery made by Applicants.

Respectfully submitted,

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Date: August 16, 2001